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## THE INVOLVEMENT OF ACTH AND MSH IN THE STRESS RESPONSE IN TELEOST FISH

by

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### ABSTRACT

Increased secretion of cortisol, the most important corticosteroid of teleost fish, is a primary indicator of stress. Although cortisol secretion is under multiple control, the pituitary gland has a dominating role. For all vertebrates ACTH is generally considered the most important factor mediating pituitary control of corticosteroid secretion during stress.  $\alpha$ -MSH may be of importance in addition to or instead of ACTH, depending on the type of stressor.

KEY WORDS:  $\alpha$ -MSH, ACTH, cortisol, stress response, teleost fish.

Traditionally, corticosteroids have been attributed a major role in stress physiology. For many vertebrates the involvement of hypothalamus and pituitary gland in the control of corticosteroid secretion has been established, with CRH, AVP and ACTH as the most important secretagogues, and cortisol or corticosterone as the adrenocortical end products of the hypothalamo-pituitary-adrenal axis (CHROUSOS & GOLD, 1992). In general, this vertebrate pattern does also apply to teleost fishes (SUMPTER *et al.*, 1994). In this paper the pituitary involvement in the control of cortisol, the main end product of the hypothalamo-pituitary-interrenal (HPI-) axis in fish, will be reviewed. In these animals the experimental evidence for a prominent role of ACTH as a corticotropic hormone during stress is in fact rather limited, and the corticotropic function of MSH may have been underestimated.

*Cortisol.* In fish, cortisol has been implicated in the formation and mobilization of energy substrates. It further stimulates the differentiation of chloride cells, the main ion-transporting cells in the gills. This effect likely is of adaptive significance, mainly because of potential damage to the gills by stressors (WENDELAAR BONGA & LOCK, 1992). Chronically elevated cortisol levels have been implicated in the reduction of growth and reproduction, as well as in immunosuppression associated with prolonged exposure to stressors. The endocrine control of cortisol secretion in teleost fish is complex. Atrial natriuretic factor,

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angiotensin II and urotensins all have direct stimulatory effects on cortisol release in trout (ARNOLD-REED & BALMENT, 1994). However, these secretagogues most likely are no more than modulating the corticotropic actions of hormone(s) originating from the pituitary gland: studies on hypophysectomized fish have indicated that the pituitary gland dominates the endocrine control of cortisol secretion (YOUNG, 1993). ACTH and  $\alpha$ -MSH are the main candidates for pituitary control.

**ACTH.** There is extensive histological evidence for the involvement of ACTH in the stress response to stressors in fish (see DONALDSON, 1981). However, few reports on plasma ACTH levels are available, because of lack of specific and sensitive assays for most species and the presence of different ACTH-like peptides released by the pituitary, as indicated by studies on goldfish, salmonids and tilapia (see BALM *et al.*, 1994). A rise of plasma ACTH immunoreactivity has been observed in salmonids subjected to handling and confinement (SUMPTER *et al.*, 1986; PICKERING *et al.*, 1987). However, thermal shock had no effect in brown trout (PICKERING *et al.*, 1986) even though plasma cortisol levels were highly elevated. BALM *et al.* (1994) recently showed that in the tilapia *Oreochromis mossambicus* two types of peptides accounted for most of the ACTH-immunoreactivity released by the pituitary pars distalis, with similar corticotropic potency. The immediate rise in cortisol following handling stress in tilapia was not preceded or accompanied by a rise in ACTH. When tilapia were confined in pairs, a detectable rise in plasma ACTH was only found in one of the animals, which also showed a higher cortisol level. In the other, perhaps socially dominant, fish of each pair, the ACTH levels were not significantly elevated, and the rise in plasma cortisol was only marginal (BALM *et al.*, 1994). These results show that the stress-related rise in cortisol in fish is not exclusively dependent on elevated plasma ACTH.

**MSH.**  $\alpha$ -MSH and  $\beta$ -endorphin are the most important hormones released by the MSH cells. Before secretion, MSH can be acetylated, a process that results in three hormonally active forms of MSH: des-, mono- and di-acetylated MSH. These forms have also been demonstrated in fish (FOLLENIUS *et al.*, 1986). Although  $\alpha$ -MSH derives its name from its capacity for pigment dispersion in skin melanophores, this action is only found in a limited number of vertebrates. Therefore, other functions of the MSH cells are indicated and several reports have suggested a role in stress adaptation. SUMPTER *et al.* (1985) showed for brown trout that plasma levels of  $\alpha$ -MSH,  $\beta$ -endorphin and cortisol were raised in fish subjected to handling and confinement combined with a thermal shock. In rainbow trout restrained out of the water, plasma ACTH,  $\alpha$ -MSH and cortisol were elevated (SUMPTER *et al.*,



1986). Acidified water activates the MSH cells and elevates plasma MSH levels (LAMERS *et al.*, 1991). All three forms of  $\alpha$ -MSH were released *in vivo* as well as *in vitro*,  $\alpha$ -MSH stimulates cortisol release from tilapia interrenal tissue incubated *in vitro*, with di-acetyl  $\alpha$ -MSH showing the highest corticotropic activity, followed by the des-acetyl and the mono-acetyl form (LAMERS *et al.*, 1992). Recently, BALM *et al.* (1995) reported that N-acetyl- $\beta$ -endorphin potentiates the corticotropic activity of  $\alpha$ -MSH in tilapia. When the concentration difference between both hormones—plasma  $\alpha$ -MSH concentrations are an order of magnitude higher than those of ACTH in trout (SUMPTER *et al.*, 1986) and tilapia (BALM *et al.*, 1995)—we may conclude that the corticotropic action of tilapia  $\alpha$ -MSH is physiologically relevant. A further indication of a role for  $\alpha$ -MSH in the HPI-axis of tilapia was the demonstration of a feedback relationship with cortisol. High cortisol levels induced *in vivo* by cortisol-containing food decreased the sensitivity of the  $\alpha$ -MSH cells to TRH 10-fold and that to CRH 100-fold (LAMERS *et al.*, 1994).

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